CARDIOVASCULAR MAGNETIC RESONANCE IMAGING IN HYPERTROPHIC CARDIOMYOPATHY: THE IMPORTANCE OF CLINICAL CONTEXT

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ABSTRACT

In patients with suspected or established hypertrophic cardiomyopathy (HCM), cardiovascular magnetic resonance (CMR) is widely employed for clinical management, given its multi-modality approach capable of providing unique information on cardiac morphology, function and tissue characterization. Guidance regarding all aspects of HCM diagnosis and management is provided by the comprehensive 2014 ESC guidelines on HCM. CMR should be performed in centres with recognized expertise in heart muscle diseases, by physicians who are familiar with the whole HCM disease spectrum, differential diagnoses and pitfalls. Because CMR is usually performed and interpreted by physicians not directly involved in patient care, detailed, bidirectional and standardized communication becomes essential to obtain best results and avoid misinterpretation. In order to maximise the potential of CMR, it is of paramount importance that reporting physicians are provided with the essential clinical information and that, in turn, referring physicians are provided a core set of CMR morphological, functional and tissue characterization results following the test. This article aims to summarise the current knowledge on the role of CMR in managing HCM and, in addition, to review the importance of the clinical context in which the report is provided, in both adult and paediatric population, highlighting implications for clinical research.

Introduction

Cardiovascular magnetic resonance (CMR) is an advanced imaging modality capable of providing unique information on cardiac morphology, function and tissue characterization. CMR is recommended in patients with suspected hypertrophic cardiomyopathy (HCM) who have inadequate echocardiographic windows, for diagnostic purposes (Class I) as well as in patients who already fulfil diagnostic criteria for HCM, for disease staging (Class IIa) (1-2). Guidance regarding all aspects of HCM diagnosis and management is provided by the comprehensive 2014 ESC guidelines on HCM (1). In addition, the 2015 EACVI expert consensus document on the role of cardiac imaging in HCM provides a wealth of recommendations on the role and appropriate use of multimodality cardiac imaging in this disease, including echocardiography, CMR, cardiac computed tomography, and cardiac nuclear imaging (3).

It is advantageous for patients that CMR is performed in centres with recognized expertise in heart muscle diseases, by physicians who are familiar with the disease spectrum and differential diagnoses including secondary remodelling or athlete's heart. Furthermore, it is advantageous that CMR not be performed or interpreted as a stand-alone test, but rather be integrated with all available pre-test diagnostic information and, when possible, interpreted based on pre-existing clinical suspicion. It is of paramount importance that reporting physicians are provided with the necessary clinical information and that, in turn, referring physicians are given a core set of morphological, functional and tissue characterization results following the test. This article aims to summarise the current knowledge on the role of CMR in managing HCM and, in addition, to review the importance of the clinical context in which the report is provided, in both adult and paediatric population, highlighting implications for clinical research.

Indications

- *Patients with a suspicion of HCM*

Echocardiography is the first line imaging modality for patients with suspected HCM, but may be limited by poor acoustic windows, particularly for near-field structures such as the cardiac apex. CMR, with its excellent spatial resolution, sharp blood pool/myocardium contrast, three-dimensional tomographic imaging, may overcome these limitations (1,3). CMR is a non-invasive test with no ionising radiation exposure and is therefore well suited for evaluating young patients with established or suspected HCM, likely to be scanned more than once in their lifetime. In patients with abnormal ECGs

(left ventricular hypertrophy -LVH-, repolarization abnormalities, Q waves, etc) but unremarkable echocardiography and no evidence of ischaemic heart disease, CMR may unmask focal hypertrophy, particularly at the level of the apex, anterior free wall and posterior septum. In about 6% of consecutive HCM patients, CMR allows detection of regional LVH missed by transthoracic echocardiography (4).

Advances in genetic diagnosis have led to the characterization of ancillary HCM manifestations in those individuals termed genotype positive-phenotype negative, who carry pathogenic mutations, but lack evidence of LVH (5). Morphological features described in "phenotype-negative" patients include myocardial crypts (6), mitral valve leaflet elongation (7), para-septal muscle bundles (8), increased extracellular volume by T1 mapping techniques (9), reduced segmental peak systolic and peak diastolic circumferential strain and regional fibrosis (3). However, identification of mild, pre-clinical phenotypes, poses new dilemmas for clinical management in these asymptomatic subjects undergoing assessment solely as relatives of an affected individual, in that their likelihood of developing overt disease is unpredictable. Non-LVH status is generally considered benign and while life-threatening arrhythmias have been reported in this subset, their occurrence is exceptional. Therefore, it may be reasonable to limit CMR to genotype-positive individuals – or family members at large if genetic test is unavailable or inconclusive, whenever an early diagnosis will have clinical implications, e.g. in the presence of unexplained symptoms, malignant family history or pre-participation in elite sporting activities (3). In addition, CMR should be considered in patients with abnormal ECG showing signs of LVH and T-wave inversion, when echocardiography is normal or inconclusive (**Supplemental Figure 1**) (3).

CMR is part of the evaluation of athletes with clinical suspicion of HCM together with comprehensive personal and family history, ECG, echocardiogram and metabolic exercise testing (1,5). A non-concentric pattern of hypertrophy, presence of typical midwall late gadolinium enhancement (LGE), perfusion defects on stress imaging, right ventricular (RV) hypertrophy, non-dilated left ventricular (LV) cavity with maximum LV wall thickness above 15 mm, elongated anterior mitral valve (MV) leaflet with or without systolic anterior motion (SAM), all point towards the diagnosis of HCM (5). Most of these features are also useful in distinguishing HCM from hypertensive heart disease. The typical LGE pattern of HCM can be helpful in this regard, although LGE may be present also in hypertensive heart disease. In the case of mild, localized subaortic hypertrophy associated with sigmoid septum in older hypertensive patients differential diagnosis may be difficult even with CMR, and relies largely on ECG, family history/screening and genetic analysis.

- Patients with an established diagnosis of HCM

CMR is well suited to describe the heterogeneous expressions of HCM ranging from typical asymmetric septal hypertrophy to apical LVH to the restrictive or dilated-hypokinetic end-stage variants **(Figure 1-2)** (2,3,10). CMR can be very useful in assessing the extent of hypertrophy in regions that are difficult to image by echocardiography, as the lateral or basal anterior LV wall or LV apex. CMR can detect apical aneurysms, describe their dimension and the presence of fibrosis and thrombi, with implications for outcome (11). CMR should be considered in all HCM patients, in absence of contraindications, local resources permitting (3).

Doppler echocardiography is the modality of choice for quantification of left ventricular outflow tract (LVOT) obstruction at rest or during provocative maneuvers or stress test. In this setting, CMR can help in assessing the etiology of difficult cases of LV outflow or midventricular obstruction, and in detecting RV outflow tract obstruction. In patients undergoing myectomy, CMR can provide precise measurements of the extent and distribution of hypertrophy, and detect the presence of MV apparatus abnormalities or accessory chordae tendineae/papillary muscles, guiding the surgical approach. MV abnormalities are frequent in HCM patients, and should be specifically investigated. Furthermore, CMR provides tomographic imaging of the complex interactions between MV, papillary muscles , and LV cavity and outflow. Compared to echocardiography, CMR is less accurate in characterizing mitral leaflets morphology and chordae, but is superior in the identification of accessory papillary muscles , their anomalous insertions and distribution and the presence of muscle bundles (3,10). CMR before invasive septal reduction therapy can help in the decision of myectomy versus alcohol septal ablation, in particular to exclude massive LVH, mid-ventricular obstruction or sub-aortic membranes in patients with suboptimal echo images.

CMR can be used to detect focal and diffuse (interstitial) myocardial fibrosis by LGE and T1-mapping techniques, respectively **(Figure 1-2)** (12). While T1 mapping is still largely limited to investigational purposes, LGE has penetrated clinical practice and adds the unique ability to detect focal scar to the CMR assessment of cardiomyopathy patients. LGE extent and distribution has been extensively evaluated in HCM, leading to the identification of typical patterns characterizing sarcomeric forms (mid-wall distribution at the basal anteroseptal level in thick-filament HCM, mid-wall but more diffuse often in atypical sites in thin filament HCM) (2). Furthermore, peculiar patterns of LGE have been identified suggesting alternative, non sarcomeric diagnoses such as Anderson-Fabry disease and amyloidosis **(Figure 3)** (1,13). Differentiation of rare genocopies is one of the main aims of CMR in newly identified patients, as their prognosis and treatment may differ radically from classic HCM (1,13).

Extensive LGE has been identified as a risk factor for sudden cardiac death (SCD) (14) and adverse remodeling (15,16), although its independent value is still debated. The largest study to date (17) showed that the extent of LGE was independently associated with SCD in a low-risk population, but this might have been driven by the presence of a limited number of outliers (18). A large international prospective registry on the prognostic role of LGE in HCM (HCMR) has completed recruitment and its results are eagerly awaited (19). LGE distribution in HCM is heterogeneous. However, the two most prevalent are the intramural, mid-wall pattern, generally located in the segments with greatest LVH, and the junctional pattern at the RV insertion points. These two patterns have different pathophysiology and prognostic value. Intramural LGE is generally considered a marker of replacement fibrosis and has been associated with SCD (17). In contrast, autopsy studies showed that RV insertion points LGE in both HCM and control subjects comprised expanded extracellular space containing interstitial fibrosis and adipose tissue, embedded with disorderly arranged myocytes, but virtually devoid of scar (20-21). Consistently, junctional LGE has no prognostic value (21). As suggested by the ESC 2014 HCM guidelines, "CMR may be considered every 5 years in clinically stable patients, or every 2–3 years in patients with progressive disease."(1) The latter indication is based on a study showing fast progression of LGE in selected patients with HCM (16). In addition, CMR can be repeated according to changes in clinical status, such as symptom progression or acute events in order to clarify modifications in myocardial function, morphology and degree of fibrosis. A recent statement of the European Medicines Agency (EMA) raises potential concerns over the repeated use of contrast CMR scanning following the detection of gadolinium deposition in the brain. There is currently no evidence that has caused any harm to patients; however EMA has recommended restrictions for some intravenous linear agents in order to prevent any risks (22). This may lead to a change in surveillance strategies in the near future.

Core information required when referring a patient for CMR

Physicians involved in the care of HCM patients should provide a fundamental set of clinical data to the CMR specialist at the time of referral, as well as a detailed indication for the test (13). These elements are of critical importance, as they may change considerably the way in which CMR is performed or interpreted. For example, the level of physical activity, particularly when intense, and history and severity of hypertension can influence cardiac mass and chamber size. ECG evidence of conduction disease, short PR interval and small QRS complexes suggest infiltrative disease, and should prompt the use of T2 weighted sequences, T1 scout and T1 mapping when available **(Figure 3)**. When extreme superior QRS axis deviation and typical facial features suggest Noonan syndrome, the RV

outflow tract and pulmonary valve need to be specifically assessed (**Supplemental Figure 2**). Echocardiographic appearance suggesting non-sarcomeric causes of HCM (concentric LVH, RV hypertrophy, increased inter-atrial septum thickness, ground-glass appearance of myocardium, pericardial effusion, restrictive filling pattern), as well as relevant laboratory data (renal dysfunction, increased CK levels, etc), should be emphasized at the time of referral. Finally, a brief outline of the clinical course and echocardiographic evolution over time is desirable, particularly in patients with end-stage HCM which may resemble other disease (eg dilated or restrictive cardiomyopathy) (1,2). A proposal for referral questionnaire containing the essential information for CMR referral is provided as supplemental material. The questionnaire can be adapted according to local resources, practical consideration and time available in real life clinical practice.

Performing CMR in patients with known or suspected HCM

The most recent advances of CMR reflect progress in its technical tools, but are seldom supported by large clinical studies and unavoidably lack longitudinal validation. Thus, the most informative sequences in clinical practice remain those used for anatomic, flow, myocardial perfusion and tissue characterization, as summarised in **Table 1**. A detailed description of comprehensive CMR assessment in HCM patients is enclosed as supplemental file. Given the dynamic and progressing nature of the disease, it is of paramount clinical relevance to obtain precise assessment of right and left ventricular volumes, wall thickness, right and left atrial area, valvular morphology and dimensions, evidence of LVOT obstruction, tissue characterization with LGE assessment (extension and distribution).

CMR offers the opportunity to assess both gross macroscopic matrix abnormalities such as replacement fibrosis - by LGE - and the extracellular volume (ECV) by T1 mapping, an emergent technique for tissue characterization, based on measurement of myocardial T1 relaxation times (23). While native (non-contrast) T1 mapping can play an important role in detection of lysosomal sphingolipid accumulation, amyloid deposits or iron overload (24-26), contrast T1 mapping allows the quantification of ECV which, in the absence of amyloid or oedema, mainly reflects collagen expansion (interstitial fibrosis), and plays a key role in the differential diagnosis of cardiac diseases mimicking HCM (**Figure 3**). Both native T1 and ECV are elevated in HCM (26), suggesting that extracellular fibrosis alone does not explain regional contractile dysfunction (27). The main limitation of T1 mapping is that it varies significantly based on field strength, scanner vendors and study protocols (28) requiring validation, in clinical use, for the specific pulse sequence and field strength used (12).

The optimal method for LGE quantification is a major unresolved issue in CMR in general, and in HCM specifically (29). Estimation of the burden of fibrosis, rather than its mere presence, seems to be the real added value of LGE studies in HCM (17). However, there is no gold standard and a very large variability of methods among centres, calling for further studies to reach international consensus. The three most validated are: the 6-standard deviation method (6SD), the Full-Width Half Maximum (FWHM) method and the Raileigh curve method. In the 6SD method the myocardial voxels are considered "enhanced" when signal intensity is ≥6 SDs greater than the mean. This method was empirically tested in ischaemic myocardial scar (30) by comparing different thresholds (2 to 8 SD above the mean) and used in many studies evaluating HCM patients. In the FWHM the enhanced area is defined using the 50% of the maximum signal found by computer-assisted window thresholding within the enhanced area. It is considered accurate for quantification of well-defined and confluent ischaemic scars, but not for the ill-defined and patchy enhancement of HCM (31). The Rayleigh curve is based on a physical rationale and, compared to the 6SD method, may more accurately reflect the burden of LGE in HCM patients (32). However, it is quite complex and requires dedicated post-processing software. Finally, in the large multicentre study by Chan et al (17), quantification of LGE was made visually by manual correction of the grey-scale window, a method previously validated in comparison with the 6SD technique. Reproducibility is an important issue for LGE quantification and its implications for risk stratification. However, available data are based on small cohorts, warranting more robust assessment in the near future.

Reporting

The CMR report summarises findings from image review and post-processing analysis and it includes a core of primary qualitative and quantitative parameters. Additional parameters may also be provided, based on local CMR laboratory protocols and technical solutions adopted in each case **(Table 2)**.

LV absolute (ml) and indexed (ml/m2) volumes and function (expressed as ejection fraction EF,%), as well as mass (g; g/m2) should be reported. In HCM patients, papillary muscles can represent a significant portion of LV mass, so they should be included in the calculation of LV mass but excluded from its volumes (33), paying particular attention that the reported normal values follow the same rule. Calculation of papillary muscles mass is feasible with many available post-processing software packages, and may be considered. Distribution of hypertrophy can be described, including quantification and

location of maximal LV wall thickness, measured in short axis cine views. When measuring septal wall thickness, it is important to pay attention in excluding myocardium from the RV (i.e. moderator band at the septal insertion) and other para-septal structures, in order to avoid overestimation. Normal LV wall physiologically decrements towards the apex; the ratio of apical to basal wall thickness needs to be reported if above 1, as this indicates relative apical LVH suggestive of apical HCM (34). The presence, location and mechanism of subaortic or midventricular obstruction can be reported. Absolute (ml) and indexed (ml/m2) RV volumes together with RV ejection fraction (%) are calculated and reported. The presence and distribution of RV hypertrophy, including the entity and location of maximum wall thickness are reported; calculation of absolute and indexed RV mass (g; g/m2) may be performed in patients with RV hypertrophy, but is not routinely done. Presence and site of RV outflow tract obstruction is included.

LV and RV regional wall motion are described; longitudinal function can be assessed indirectly by the analysis of atrioventricular plane motion in systole and diastole; a more sophisticated assessment of longitudinal function may be obtained by strain analysis with dedicated software. Patients with HCM may show dysmorphic ventricles with areas of significant wall thinning, trabeculations and crypts; these findings are described and regional thinning (including minimum thickness) is reported. Apical aneurysms have a negative prognostic impact (11), so their presence, dimensions and the detection of thrombus are described in detail. Atrial dimensions, particularly the left atrium, has also been related to prognosis (1): thus, atrial area (absolute and indexed, cm2 and cm2/m2) in 4 chamber is reported, while atrial volumes may be calculated. Mitral leaflet and papillary muscle abnormalities are critical determinants of LV outflow obstruction and are accurately reported. Direct papillary implantation of the papillary muscle to mitral leaflets is reported and may guide treatment if invasive procedures are planned. Severe valvular and subvalvular abnormalities advise against referral for alcohol ablation, tilting the balance in favour of surgery. In general, a multimodality imaging approach is crucial to surgical planning for potential septal reduction therapy candidates (3,10,35,36). Evidence of LGE is described with accurate assessment of spatial distribution and extension. For those centres without quantitative software for LGE, a qualitative analysis of hyperenhancement (diffuse vs confluent) and of different subtypes (intramural, RV junction, subendocardial) can be used. Finally, accurate assessment of LGE distribution is fundamental, while calculation of its total volume, absolute or expressed as a proportion of LV myocardium, currently lacks of standardization. Quantitative assessment of native T1 mapping (in ms) and ECV (% of LV mass) is not, at present, routinely performed, although this is a rapidly evolving field (12).

Paediatric Population

Paediatric cardiomyopathies represent a very heterogeneous group of inherited heart muscle diseases, including conditions that are confined to the heart (sharing the same genetic causes as adult cardiomyopathies) as well as cardiac involvement in the context of complex syndromes (malformation syndromes, inborn errors of metabolism, neuromuscular disease, chromosomal abnormalities). Outcomes vary greatly by etiology, and HCM patients with an inborn error of metabolism or malformation syndrome (particularly, Noonan syndrome and other RASopathies) represent a high risk cohort with reduced survival (37). Consequently, an early etiologic diagnosis is fundamental to define outcome and management in children with HCM (13) (**Supplemental Figure 2**). CMR is rapidly establishing its clinical role in paediatric heart muscle diseases and appears indicated in suspected HCM, particularly when first line tests fail to reach a diagnosis (38). The diagnosis of paediatric HCM is based on the detection of LV wall thickness more than two standard deviations greater than the predicted mean for body surface area, in the absence of another cardiac or systemic disease capable of producing similar magnitude of hypertrophy (1). However, a Z-score (number of standard deviations from the mean a data point is) of 2 for maximum LV wall thickness has been criticized as being too sensitive (and poorly specific) in children when compared to the adult diagnostic threshold of 15 mm. CMR may be challenging in children because of small-sized cardiac structures, rapid heart rates and lack of cooperation with breath-holding instructions. Children unable to provide the cooperation required for an adequate scan should be scheduled for deep sedation or general anaesthesia. In infants younger than 6 months, acceptable sedation may be achieved by scanning immediately after feeding. Acquisition with navigator-gating of the diaphragm is preferred in poor breath-holders. Scan protocol is tailored to answer the specific clinical question, keeping the duration of the study to a minimum. Image parameters are adapted to reduce the acquisition time while maintaining adequate quality. With small children, high in-plane spatial resolution of up to 1 mm may be required by setting a small field of view along with a large matrix. Slice thickness is also reduced to 3–5 mm. To maintain adequate signal to noise ratio after these adaptations, the use of a small multi-element phased-array coil is typically needed. As long as the relevant diagnostic information are preserved, the application of single-shot techniques, high acceleration factors, multiple signal averaging and real-time sequences may be convenient.

Implications for clinical research

CMR, despite the well-known practical and economic limitations, has enormous potential for research. Anatomic and functional detail, tissue characterization (by LGE and T1 mapping),

quantification of myocardial blood flow, studies of energetic metabolism (by spectroscopy), assessment of fibrosis and diastolic function, are only some of the applications that can be exploited for investigational purposes in HCM, providing an unparalleled comprehensive view of the disease. However, two fundamental advances are still needed in order to achieve a real breakthrough:

1) Standardization. As large international registries and multicentre studies become a reality (www.theshareregistry.org; http://hcmregistry.org/), there is increasing need for investigators to adopt uniform clinical and imaging protocols in order to merge the information into common databases. This is often achieved by creating core labs, with the obvious advantage of eliminating local interpretation bias. However, standardization of CMR protocols at each participating centre (particularly urgent at this stage for LGE quantification) is fundamental to allow correct exchange of information, uniform management and clinical decision-making, and further expand research collaborations. As discussed, this applies to each step from selection of patients to CMR protocols to interpretation and reporting. In the research setting, this fundamental issue requires dedicated core labs.
2) Multimodality integration with other techniques providing complementary information. An important limitation of CMR lies in the fact that the technique is often reported in isolation, with little integration of clinical and functional data. In the case of LGE, for example, substrate remodeling and fibrosis are likely to become clinically useful (and achieve sufficient predictive value) only when combined with other features accounting for the extreme individual variability of the disease, including electrophysiologic properties, gene-specific energetic profile and coronary microvascular function. Recently, Arevalo et al. have proposed a three-dimensional model of post-myocardial infarction hearts integrating CMR data, estimated fiber orientation based on a geometry-driven rule-based approach, and region-specific electrophysiological properties (39). In a proof-of-concept retrospective study, this model proved superior to several existing clinical metrics in identifying patients at risk of ventricular arrhythmias. The study illustrates the potential of CMR when integrated with other instrumental modalities, in a true effort to promote personalized medicine.

Conclusions

CMR is rapidly becoming the new gold standard for the diagnosis and assessment of HCM, and its potential for further development remains impressive. However, with all its advanced technology,

CMR provides only a piece of a complex puzzle. Solely by combining the wealth of data provided by time-honored clinical, ECG and echocardiographic assessment can its potential be fully exploited. Because CMR is usually performed and interpreted by physicians not directly involved in patient care, detailed, bidirectional and standardized communication becomes essential to obtain best results and avoid misinterpretation, benefitting patient care and translational research alike. This article aims to show how clinical information and CMR findings can be integrated, by reviewing the current knowledge on indications, performing, interpreting and reporting of CMR in patients with HCM for both referring physicians and CMR specialists.

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Figure Legends

Figure 1. Standard CMR imaging in a patient with hypertrophic cardiomyopathy. Steady-state free precession (SSFP) cine (end-diastolic frame). Clockwise from top-left: short axis (**Fig 1a**), 3 Chamber (**Fig 1b**), 2 Chamber (**Fig 1c**) and 4 chamber (**Fig 1d**) views. **e-h)** Phase Sensitive Inversion Recovery (PSIR) images showing typical patchy late gadolinium enhancement (same patient and same views from Figure 1a-d). **Abbreviations: Ao:** Aorta Ch: Chamber; **IVS:** interventricular septum; **LA:** left atrium; **Laa:** left atrial appendage; **LV:** left ventricle; **lvot:** left ventricular outflow tract; **RA**: right atrium; **RV:** right ventricle.

Figure 2. Advanced tissue characterization and imaging in a patient with hypertrophic cardiomyopathy a) Steady-state free precession end-diastolic short axis cine image. **b)**STIR T2w image, showing hyperintense signal of the septum and anterior wall (arrows) **c)** Late-enhancement imaging, showing diffuse enhancement, more evident in the septum and anterior wall (arrows) **d)** Late-enhancement quantification using a commercially available software (cut-off 6SD) resulting in a 33.3% of hyper-enhancement of the total cardiac mass. Pre (**e**) and post-contrast (**f**) MOLLI T1 mapping, showing signal inhomogeneity within the septum (arrows), corresponding to extensive late-enhancement (c and d). Stress (**g**) and rest (**h**) perfusion CMR. Extensive subendocardial perfusion defect (arrows) during stress with adenosine is present (**g**).

Figure 3. Role of CMR in the differential diagnosis in hypertrophic cardiomyopathy (HCM). a-c) Cardiac amyloidosis. **Fig 3a**, steady-state free precession (SSFP) cine; **Fig 3b**, subendocardial late gadolinium enhancement (LGE); **Fig 3c**, histology from endomyocardial biopsy, positive to Congo Red staining (courtesy Dr Andrea Gianatti, Pathology Department ASST Papa Giovanni XXIII, Bergamo, Italy). **d-f) Danon (LAMP2) disease. Fig 3d**, steady-state free precession (SSFP) cine; **Fig 3e and Fig f** show extensive LGE in an atypical location for sarcomeric HCM. **g-l) Fabry disease. Fig 3g and Fig 3h**, steady-state free precession (SSFP) cine showing concentric hypertrophy; **Fig 3i an Fig 3l**, showing LGE in the basal infero-lateral wall. **m-p) Cardiac Fibroma**. **Fig 3m:** steady-state free precession (SSFP) cine showing asymmetrical septal "hypertrophy", indistinguishable from HCM. **Fig 3n** STIR T2Weighted showing inhomogeneous hypointese signal within the core of the septal mass; **Fig 3o and Fig 3p** showing intense LGE with well-defined border and a dark core, typical for cardiac fibroma (courtesy Prof James Moon, Barts Heart Centre, St Bartholomew's Hospital, West Smithfield, London, UK).

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